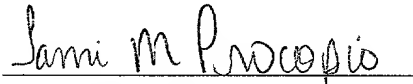


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Tami M. Procopio

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In the application of:

Chaitan Khosla, *et al.*

Serial No.: Divisional of 09/434,289

Filing Date: Even Date Herewith

For: METHOD TO PRODUCE NOVEL  
POLYKETIDES

Examiner: Unassigned

Group Art Unit: Unassigned

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

**AMENDMENT**

Please amend the specification as follows:

On page 1, line 4, after "This application is" please insert -- A divisional of US Serial No. 09/434,289 which is a continuation of U.S. Serial No. 08/896,323, filed 17 July 1997 and now U.S. Patent 6,066,721 which is --.

On page 1, line 5, please insert after "1996" -- now U.S. Patent 6,080,555, --.

On page 2, lines 6, 9, 22 and 23, please change "et al." to -- *et al.* --.

On page 3, line 9, please change "overmectin" to -- "avermectin --.

On page 4, line 19, please change "may, represent" to -- be --.

On page 5, line 10, please change "Streptomyces coelicolor" to --*Streptomyces coelicolor*--.

On page 5, line 11, please insert, before "WO95/08548" the phrase --PCT publication--.

On page 5, line 14, please change "application" to --PCT publication--.

On page 5, line 20, please delete "cys-ser-ser-ser-leu" and insert, after "alanine." --The signature sequence consists of 3 serine residues bracketed at the N-terminus by cysteine and at the C-terminus by leucine.--

On page 5, line 24, please change "Biochemistry" to --*Biochemistry*--.

On page 5, line 26, please delete "set forth below".

On page 6, line 3, please change "CH99" to --CH999--.

On page 6, line 11, please change "mL" to --  $\mu$ L-- (3 occurrences).

On page 6, line 19, please insert, before "plasmid pCK7" --a derivative of--.

On page 6, line 19, please insert after "pCK7" the phrase --(Kao, C.M., *et al.*, *Science* (1994) 265:509-512)--.

On page 6, line 20, please insert --renamed-- before "pJRJ2."

On page 6, lines 21-22, please delete "(Kao, C.M., *et al.*, ... 409-512)."

On page 6, line 22, please insert --transformants-- before "grown."

On page 7, at lines 4, 7, 14 (two times), 16, 17 and 18, please change "substrate" to --compound-- or "substrates" to -- compounds--.

On page 7, line 8, please delete "above, " and insert --above)--.

On page 7, line 18, please delete "." after "product 7".

On page 8, line 5, please change "erthromycin" to -- erythromycin--.

On page 8, lines 6, 9 and 21 and on page 9, line 1, please change "*erythrea*" to --*erythraea* --

Please amend the claims as follows:

Please cancel claims 1-17 and substitute the following claims:

18. A method to prepare a modified nucleic acid molecule, said nucleic acid molecule comprising a nucleotide sequence encoding at least a first and second module of a modular PKS, wherein said first module is immediately N-terminal to said second module and wherein said nucleotide sequence comprises a mutation such that the catalytic domain of the ketosynthase of the first module of said encoded PKS is inactivated, said encoding nucleotide sequence operably linked to control sequences for its expression,

which method comprises effecting said mutation in said nucleic acid molecule.

19. A method to prepare an antibiotic which method comprises adding a macrolide to the culture medium of *Saccharopolyspora erythraea*;

culturing said *S. erythraea* in said medium so as to convert said macrolide into an antibiotic; and

extracting the antibiotic from the medium.

20. The method of claim 37 wherein the *S. erythraea* is a mutant that produces no macrolide.

21. The method of claim 38 wherein said *S. erythraea* mutant is mutant A34.

22. The method of claim 39 wherein said macrolide is other than 6-dEB.

23. The method of claim 39 wherein said macrolide is a 14-member macrolide.

### REMARKS

This application is a divisional of U.S. Serial No. 09/434,289. In that application, original claims 1-17 were cancelled and ultimately replaced by new claims 27-42; the claims presented here are claims 36-42 proposed in the parent application which represent a non-elected invention in response to a restriction requirement wherein applicants elected to prosecute the invention of claims 27-35. No new matter has been added and entry of the amendment is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 300622000213. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: May 29, 2001

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